Pattern of Hemoglobin and Anemia in Patients Seen with Symptoms of Bladder Outlet Obstruction (BOO) at First Presentation and Review of Possible Causes of Anemia in BOO Patients

Elijah Udoh*, Felix Olisaeke

1Urology Unit, Department of Surgery, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria. *Department of Obstetrics and Gynaecology, University of Uyo Teaching Hospital, Akwa Ibom State, Nigeria

ABSTRACT

Objective: To study the pattern of hemoglobin levels in patients seen with symptoms of bladder outlet obstruction at first presentation to our facility and to review the possible causes of low hemoglobin in this group of patients. Materials and Methods: A retrospective study of hemoglobin levels in 110 patients who presented between January 1, to December 31, 2014, aged between 50 and 85 years. Information were retrieved from case notes. Hemoglobin was tested on presentation and was classified based on National Cancer Institute grading of anemia into, no anemia, mild, moderate, severe and life threatening anemia. Patients were predominantly diagnosed with benign prostatic hyperplasia, cancer of the prostate, bladder cancer and urethral stricture. Results: Of the 110 patients evaluated for hemoglobin levels and classified into different levels of severity of anemia, 30 patients were normal while 80 patients were anaemic; comprising 34 patients (31.0%) with mild, 27 patients (24.5%) with moderate, 11 patients (10.0%) with severe and 8 patients with life threatening anemia respectively. Conclusion: Low level of hemoglobin or anemia can be manifested in the setting of bladder outlet obstruction from any cause. Possible pathophysiological mechanisms have been known and well studied.

Keywords: Hemoglobin, Anemia, Bladder outlet obstruction, National cancer institute grading of anemia

Introduction

Hemoglobin (Hb) is the red oxygen carrying pigment in the red blood cells of vertebrates. It has a molecular weight of 64,450 and is made up of 4 sub-units. Each of these sub-units contains a haem moiety conjugated to a polypeptide. Haem is iron containing while the polypeptide is the globin portion of the hemoglobin. There are two types of polypeptide namely the alpha chain and the beta chain containing 141 and 146 amino acids respectively. This is the adult hemoglobin. Other variants of Hb in adults are HbA, and HbA1c. HbA1c has glucose attached to the terminal valine in each beta chain and it is important in glucose monitoring in diabetics. When the Hb level is low and hence its oxygen carrying capacity is insufficient to meet the body's physiologic needs, it is termed anemia.

Bladder outlet obstruction from any cause can lead to low levels of Hb and hence it's oxygen carrying capacity. In this study, the various causes of bladder outlet obstruction were; cancer of the prostate, benign prostatic hyperplasia, urethral stricture and cancer of the bladder. In the literature review, the possible causes of low Hb or anemia in patients with bladder outlet obstruction ranged from blood loss, anemia of chronic disease, chronic renal failure and bone marrow infiltration by malignant cells thereby halting erythropoiesis.
Materials and Methods

This was a retrospective study of hemoglobin level of patients who presented to us with symptoms of bladder outlet obstruction from January 1st to December 31st, 2014. Information was retrieved from their case notes. They were seen either in Accident and Emergency or Surgical Outpatient Department. Their hemoglobin levels were determined on first presentation and used for this study. A total of 110 patients were seen and blood samples taken for Hb estimation. They were all males ranging from 50 to 85 years with a mean age of 67.5 years.

The pattern of Hb and anemia was classified according to the National Cancer Institute classification and grading of anemia as follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of anemia</th>
<th>Hemoglobin values (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Within normal limits</td>
<td>12.0-16.0 (women) 14.0-18.0 (men)</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>10.0 to levels within Normal limits</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>8.0-10.0</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>6.5-7.9</td>
</tr>
<tr>
<td>4</td>
<td>Life threatening</td>
<td>&lt;6.5</td>
</tr>
</tbody>
</table>

Results

Analysis showed that, of the 110 patients; 30 patients representing 27.3% had Hb levels above 14.0g/dl and were not classified as anemic while 80 patients representing 72.7% were classified anemic at various levels of severity. Further analysis of the latter group showed that 34 patients (31.0%), 27 patients (24.5%), 11 patients (10.0%) and 8 patients (7.2%) were classified as mild, moderate, severe and life threatening anemic patients respectively Table 1, Figures 1 and 2.

Discussion

Hemoglobin (Hb) concentration in the body can be affected adversely by both genetic and acquired conditions. In bladder outlet obstruction (acquired condition) characterized by difficulty with emptying of urinary bladder content and subsequent complications in the bladder, ureters and kidneys can affect the Hb concentration of the blood. The mechanism is multifactorial. Back pressure of urine to the kidneys causing hydronephrosis will lead to progressive atrophy of the renal parenchyma and renal failure. Patients suffering from renal failure almost invariably develop anemia to a greater or lesser extent which is largely due to inappropriate erythropoietin production. Erythropoietin is produced by the peritubular cells of the kidney. In renal insufficiency, the cells are gradually lost and hence the ability of the kidneys to respond to a progressively anemic state is reduced. This in turn causes a reduction in erythroid cell proliferation and differentiation in the bone marrow and eventually a low circulating red cell mass.

In addition to low levels of erythropoietin in this set of patients, there are many other factors contributing to the anemia of renal failure. These include; haematinic deficiency; particularly iron and folic acid, low grade haemolysis, blood loss particularly from the gastrointestinal tract and suppression of erythropoiesis by uraemic inhibitors. The concepts of uraemic inhibitors have been a subject of much current interest. These substances inhibit erythropoiesis and include polyamines, parathyroid hormone and some of the inhibitory cytokines. The role of these substances remains a mystery. Since the early 1970’s, it has been suggested that polyamines may play
a role in the pathogenesis of anemia in renal failure. Polymamines are series of organic cations; and include substances such as spermine, spermidine, putrescine and cadaverine. They are believed to play a role in cellular proliferation and differentiation. It is also known that they accumulate in the plasma of patients with chronic renal failure and have been found to reduce proliferation and maturation of erythroid cells. There is reasonable evidence to suggest that polymamines may exert a specific inhibitory effect on erythropoiesis. This suppression of bone marrow activity seemed fairly specific to the erythroid lineage since leucopenia and thrombocytopenia are not usually seen in renal failure.

The role of parathyroid hormone either directly or indirectly modulating erythropoiesis has also been a subject of clinical debate. In renal failure patients, it has been suggested that hyperparathyroidism is one of the causes of poor response to erythropoietin therapy; and possible explanations for this phenomenon include development of marrow fibrosis and a direct effect of parathormone in suppressing erythroid colony growth. Inflammatory cytokines have also been implicated as modulators of erythropoiesis in uremic patients. These cytokines; interleukin-2 (IL-2), interleukin-3 (IL-3), insulin-like growth factor-1 (IGF-1) may enhance erythropoiesis by promoting the differentiation of primitive erythroid cells from the precursor stem cells thus increasing the pool of cells on which erythropoietin can act on. The pro-inflammatory cytokines, on the other hand, namely interleukin-1 (IL-1), tumour necrosis factor-α (TNF-α) and interferon-γ(IF-γ) have inhibitory effects on erythropoiesis. Allen et al demonstrated that the inhibitory effect of uraemic serum on human erythroid colony growth could be partially or completely reversed by pre-exposure to a polyclonal antibody against tumour necrosis factor-α or interferon-γ. The combination of these antibodies was additive, suggesting that both cytokines may be involved in this process.

Urinary tract stones caused by precipitation of crystals in the kidneys, ureters or bladder consequent upon stasis from bladder outlet obstruction can cause microhaematuria in about 85% of cases but gross haematuria tends to be rare.

A case of acute haemolytic anemia caused by E Coli Urinary tract infection was reported by Herbert T. et al which cessation of haemolytic process was demonstrated to coincide with the introduction of appropriate antibiotic therapy. This could co-exist in patients with bladder outlet obstruction who present with low hemoglobin. Aside from the general effects of stasis and back pressure of urine to the kidneys caused by bladder outlet obstruction, specific actiologies of bladder outlet obstruction can pose specific problems. In carcinoma of the prostate (Cap) especially in advanced stage, anemia could be caused by androgen deprivation, bone marrow replacement, anemia of chronic disease, inflammatory cytokines, haematuria and poor nutrition. Some of the patients seen with prostate cancers must have been previously exposed to androgen deprivation before presenting to us and an androgen deprivation therapy (ADT) is a well documented cause of anemia as testosterone is required for enhancement of erythropoietin formation in the kidneys as well as bone marrow action of erythropoiesis. Jeffrey et al also pointed out that replacement of bone marrow with cancer cells also contribute to low hemoglobin in men with cap due to impaired haematoipoiesis.

Anemia of chronic disease is a form of anemia seen in chronic infection, chronic immune activation and malignancy. These conditions also produce massive elevation of interleukin-6 (IL-6). In response to increasing interleukin-6 production, the liver produces increased amount of hepcidine which in turn causes increased internalization of ferroportin molecules in cell membrane which prevents release of iron stores. Inflammatory cytokines also appear to affect other important elements of iron metabolism including decreasing ferroportin expression and probably directly blunting erythropoiesis by decreasing the ability of the bone marrow to respond to erythropoietin.

In anemia of cancer as in anemia of chronic disease, multiple mechanisms can interfere with normal erythrocyte production. The cytokines TNF-α, TGF-β, IL-1, IL-6 and interferon-γ are likely most prevalent as inhibitory mechanisms. This network of cytokines probably modulates iron metabolism and the erythropoietin effect may be blunted by TNF-α among others. An anti-TNF-α antibody may abrogate this effect and has been demonstrated in rheumatoid arthritis. Moreover, activation of macrophages can lead to a shorter erythrocyte half-life and a decrease in iron utilization. Drug therapy further aggravates anemia in cancer patients such as radiotherapy and chemotherapy.

Nutritional decline may also lead to low hemoglobin in patients with cancer. Haematuria can contribute to this phenomenon due to cancer infiltration of the urethra and bladder wall as in prostate cancers and bladder cancer with consequent sloughing and bleeding. In BPH as well as in prostate cancer, grossly, there is increased density of the micro-vessels in the prostate and in a 2002 cross sectional study, had a self reported rate of haematuria in 2.5% of subjects with BPH.

In our study as well as other studies reviewed, patients presentation is usually late and most of these mechanisms causing low hemoglobin level go on unchecked. Only 30 patients representing 27.3% of all patients evaluated had their hemoglobin levels within normal limits while 72.7% were anemic at various levels of severity. Severe and life threatening anemia seen in 17.2% of the population studied carry grave consequences if not adequately addressed especially in other poor resource centres with no facilities for blood transfusion. The progressive nature of the pathologies, even in the mild to moderate groups, is a cause for concern. In all of these situations, addressing the underlying pathologies early and promptly and correction of anemia is the key to successful management.

Conclusion

Low hemoglobin in patients with bladder outlet obstruction causes significant morbidity. It impairs virtually every organ and tissue of the body leading to multiple function disturbances, decreasing mental and physical performance capacity. Most of the patients in the study presented late and the underlying pathophysiological changes continue unannounced until bladder outlet obstructive symptoms brought them to our facility.

With the knowledge of this study, awareness campaign can evolve to sensitize men in this age group to seek medical care at the earliest notice of symptoms to forestall attendant morbidity and mortality that come with late presentation accessioned by high prevalence of low hemoglobin and other complications.

References


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